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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER

ART UNIT	PAPER NUMBER
	8

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No	Applicant(s)
09/238,741	Braslawsky et al
Examiner	**Art Unit**
Larry R. Helms Ph.D.	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *25 Apr 2001*

2a) X This action is **FINAL.** 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *1-49* is/are pending in the applica

4a) Of the above, claim(s) *3, 10-13, 15-23, 30-33, 38-40, and 42-44* is/are withdrawn from considera

5) Claim(s) _____ is/are allowed

6) X Claim(s) *1, 2, 4-9, 14, 24-29, 34-37, 41, and 45-49* is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirem

Application Papers

9) The specification is objected to by the Examiner

10) The drawing(s) filed on _____ is/are objected to by the Examiner.

11) The proposed drawing correction filed on _____ is a) approved b) disapproved

12) X The oath or declaration is objected to by the Exam iner

Priority under 35 U.S.C. § 119

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d)

a) All b) Some* c) None of

1 Certified copies of the priority documents have been received

2 Certified copies of the priority documents have been received in Application No _____

3 Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

DETAILED ACTION

1. Claims 1-49 are pending.

Claims 47-49 have been added.

Claims 1, 5, 7, 9, 24, 28, 37, 41, 45, 46 have been amended.

2. Claims 3, 10-13, 15-23, 30-33, 38-40, 42-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions. Election was made **without** traverse in Paper No 4.

3. Claims 1-2, 4-9, 14, 24-29, 34-37, 41, 45-49 are under examination.

4. The text of those sections of title 35, USC Code not included on the Office Action can be found in a prior Office Action.

5. The following contains some NEW GROUNDS of rejection.

Oath/Declaration

6. The Examiner acknowledges that a new Declaration will be submitted in due course, however, the oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

"V" with a "J". In addition the name "Garry R. Braslawsky has been altered to "Gary Ronald Braslawsky"

Claim Objections

7. Claims 28 and 41 are objected to because of the following informalities: Claim ~~41 is~~ dependent on ~~no elected~~ claim 22. Appropriate correction is required.

Rejections Withdrawn

8. The rejection of claims 1-2, 4, 5-9, 24-29, 34, 36, 37, 45 and 46 under 35 U.S.C. 112, second paragraph, for paragraph 8a, c, d, e-g, j-m in the previous Office Action, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

Response to Arguments

9. The rejection of claims 1-2, 4, 5-9, 24-29, 34, 36, 37 and newly submitted claims 47-49 under 35 U.S.C. 112, second paragraph, for paragraphs 8b, h-l in the previous Office action, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

The response filed 4/25/01 has been carefully considered but is deemed not to be persuasive. The response states that "desired binding specificity" is clear and definite and "any antibody that binds to an antigen with specificity can benefit from the method". In response to this argument, it is still unclear if the phrase means that the antibody has specific binding or if it is hoped to have a specific binding. The response further states that "C2B8/p5E8" is defined in the subject application and US Patents 5,830,698 and 6,011,138 provide discussion of the antibodies. In response to this argument, it is still unclear if these antibodies are those recited in the claims. Amending the claims to recite the ATCC number of the hybridoma or the SEQ ID Nos for the heavy and light chains is requested.

10. The rejection of claims 1-2, 4, 5-9, 24-29, 34, 36, 37, 45 46 , and newly submitted claims 47-49 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing a IgG antibody heterodimer with antibodies which specifically bind CD20 and CD23(p5E8) comprising obtaining or constructing a DNA molecule that encodes an antibody that binds antigen and comprises a heavy chain and a light chain with the same antigen binding specificity, wherein the heavy chain has a cysteine residue introduced at position 444 (Kabat numbering) that does not interfere with antigen binding or proper folding and compositions comprising [illegible] anti-CD20 anti-CD23 [illegible]

any IgG antibody heterodimer wherein the antibody does not bind antigen, comprises a light

chain from any antibody paired with any heavy chain wherein the heavy chain contains a cysteine residue introduced anywhere even in the CDRs and pharmaceutical compositions comprising such and wherein the antibody heterodimer initiates apoptosis or complement mediated cell killing in any cell is maintained.

The response filed 4/25/01 has been carefully considered but is deemed not to be persuasive. The response states that the disclosure fully satisfies the enablement standard (see page 10 of response). In response to this argument, the response does not address the art of Rudikoff et al cited for providing the requirements of a complete antigen binding site. The claims still encompass antibodies with heavy chains and any light chain paired with the heavy chain. The claims still encompass a cysteine residue introduced anywhere in the heavy chain, even in the CDRs. In addition, the response states that "the advantages of the invention are obtained by using monoclonal antibodies which had had a cysteine residue genetically engineered at a specific site on the Fc arm of the antibody" (see page 10-11 bridging paragraph). In response to this statement, the examiner has acknowledged that the specification is enabled for a cysteine residue at position 444 in the Fc region.

11. The rejection of claim 35 under 35 U.S.C. § 112, first paragraph, because the

that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description is maintained.

The response filed 4/25/01 has been carefully considered but is deemed not to be persuasive. The response states"those skill in the art have access to US Patent 5,830,698 and 6,011,138 which are of record in the subject application" (see page 10 of response). In response to this argument, it is still not clear if the hybridomas that produce the antibodies are commercially available.

12. The rejection of claims 2, 4, 28, 41, and 46 under 35 U.S.C. 102(b) as being anticipated by Brennen et al (Science 229:81-83, 1985) is maintained.

The response filed 4/25/01 has been carefully considered but is deemed not to be persuasive. The response states Brennan et al does not disclose each feature such as "formed by linking two antibody molecules". In response to this argument, Brennan et al teach an antibody dimer formed by linking two antibody molecules. The claims do not recite an antibody tetramer is produced. The claims recite obtaining one heavy chain with a cysteine residue introduced and one light chain and reducing and obtaining a heterodimer. Brenner et al teach a heterodimer. Thus, the art reads on the claims. "Even though product-by-process claims are limited by and

product-by-process claim I is the same or obvious from a product of the prior art, the claim is

unpatentable even though the prior product was made by a different process." *In re* Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113.

13. The rejection of claims 1-2, 4-9, 14, 24-29, 34-37, 41, 45-46 and newly submitted claims 47-49 under 35 U.S.C. 103(a) as being unpatentable over Caron et al (J. Exp. Med. 176:1191-1195, 1992) and further in view of Fanger et al (Critical Reviews in Immunology 12:101-124, 1992) and Cumber et al (J. Of Immunol. 149:120-126, 1992) and Reff et al [a] (U.S. Patent 6,011,138, filed 2/20/97) and Reff et al [b] (Blood 83:435-445, 1994) is maintained.

The response filed 4/25/01 has been carefully considered but is deemed not to be persuasive. The response argues that Caron et al does not disclose or suggest each feature of the present invention and continues to argue the references separately. In response to applicant's arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In response to arguments that there is no suggestion to reduce the intra or inter molecular disulfide bonds, Cumber et al teach specifically reducing the disulfide linked dimer to monomers (see page 121 under synthesis). In addition, Fanger et al teach an

motivation to reduce the disulfide bonds that are intra or inter for coupling to produce antibody dimers as claimed.

The following are some NEW GROUNDS of rejections

Claim Rejections - 35 USC § 112

14. Claims 1-2, 4-9, 14, 24-29, 34-37, 41, 45-49 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claims fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in Paper No. 7 filed 4/25/01. In that paper, applicant has stated "By using special conditions (i.e., purifying the selectively reduced monoclonal antibody by applying it to PD-10: and equilibrating with the oxygenated normal saline containing sodiumcitrate, which discourages the formation of homodimer via disulfide bond) one can be assured that only dimers formed by thioether linkage are produced." (See page 11), and this statement indicates that the invention is different from what is defined in the claim(s) because the claims do not recite this special conditions or method of purification.

15. No Claims are allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D. whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a

18. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879

Sheela J Huff

SHEELA HUFF
PRIMARY EXAMINER